

筒井和義 教授 略歴・業績

筒井和義 (1952年生) 67 歳

早稲田大学教育・総合科学学術院／大学院先進理工学研究科／先端生命医科学センター・教授

◆ 最終学歴 ◆

1981年 3 月 早稲田大学大学院理工学研究科博士課程後期修了 (理学博士)

◆ 略歴 ◆

83. 3-91. 3 広島大学理学部動物学科助手

91. 4-93. 1 神戸大学医学部講師

93. 2-96. 9 広島大学総合科学部助教授

96.10-06. 8 広島大学総合科学部教授

00. 4-現在 財団法人 (現公益財団法人) サントリー生物有機科学研究所アドバイザー (兼任)

03. 4-06. 8 広島大学統合脳科学プロジェクト研究センター長 (兼任)

06. 9-現在 早稲田大学教育・総合科学学術院／大学院先進理工学研究科／
先端生命医科学センター教授

13. 3 広島大学名誉教授

◆ 主な研究業績 ◆

生体調節, 本能と意欲, 記憶・学習の新しい脳制御機構の解明を目指し, 重要な新規脳ホルモンの同定とそれらの生理機能, 作用機構, 発現制御機構を解析している。この過程で, 動物の生殖を抑制する新規脳ホルモンである生殖腺刺激ホルモン放出抑制ホルモン (GnIH) を発見した。生殖機能異常症の新しい治療薬の開発を目指している。一方, 動物の脳がステロイド (ニューロステロイド) を合成することを見いだした。ニューロステロイドはニューロンの発達やシナプスの形成を誘導することを明らかにした。また, 動物の活動性を高める新規のニューロステロイドを発見し, この新規ニューロステロイドの働きにより活動性の日内リズムが形成されることを明らかにした。

◆ 英文発表論文 (最近 10年間の抜粋) ◆

Haraguchi et.al. (2019) *eLife* 8: e45306

Tsutsui et al. (2017) *Endocrinology* doi: 10.1210/en.2017-00300 (review)

- Kriegsfeld et al. (2015) *Front. Neuroendocrinol.* 37: 65–75 (review)
- Ubuka et al. (2014) *Nature Communications* 5: Article number 3061 doi: 10.1038/ncomms4061
- Tsutsui et al. (2013) *Front. Neuroendocrinol.* 34: 179–189 (review)
- Maekawa et al. (2013) *Nature Communications* 4: Article number 1372 doi: 10.1038/ncomms2372
- Haraguchi et al. (2012) *Proc. Natl. Acad. Sci. USA* 109: 21110–21115
- Hatori et al. (2011) *Proc. Natl. Acad. Sci. USA* 108: 4864–4869
- Tsutsui et al. (2010) *Front. Neuroendocrinol.* 31: 284–295 (review)
- Doi et al. (2010) *Nature Medicine* 16: 67–74
- Tsutsui (2009) *Prog. Neurobiol.* 88: 76–88 (review)
- Do Rego et al. (2009) *Front. Neuroendocrinol.* 30: 259–301 (review)
- Tsutsui et al. (2008) *J. Neuroscience* 28: 2158–2167
- Tsutsui (2008) *Endocrinology* 149: 2757–2761 (review)
- Sasahara et al. (2007) *J. Neuroscience* 27: 7408–7417
- Kriegsfeld et al. (2006) *Proc. Natl. Acad. Sci. USA* 103: 2410–2415
- Ubuka et al. (2005) *Proc. Natl. Acad. Sci. USA* 102: 3052–3057 *Nature Reviews Highlight*
- Matsunaga et al. (2004) *Proc. Natl. Acad. Sci. USA* 101: 17282–17287

原著・総説論文総数 535 編 国際会議基調・招待講演 101 回 *h-index* 65

◆ 英文著書（最近 10 年間の抜粋）◆

- The E-Book: Frontiers Research Topic on The Roles of GnIH in Reproductive* Published in *Frontiers in Endocrinology*, 126 pp., 2018
- Special Issue of Tsutsui Profiles in Comparative Endocrinology* Published in *Gen. Comp. Endocrinol.*, 142 pp., 2016
- Handbook of Hormones: Comparative Endocrinology for Basic and Clinical Research* Published by Elsevier publisher, 646 pp., 2015
- Special Issue of the 10th International Symposium on Avian Endocrinology* Published in *Gen. Comp. Endocrinol.*, 235 pp., 2013
- The E-Book of Neurosteroids: Frontiers Research Topic* Published in *Frontiers in Endocrinology*, 476 pp., 2013

◆ 邦文著書（最近 10 年間の抜粋）◆

- シリーズ 21 世紀の動物科学：内分泌と生命活動 日本動物学会監修 培風館 2007

◆ 主な受賞暦 ◆

動物学会賞 2001（日本動物学会）
 吉村賞 2008（日本下垂体研究会）
 Farner Medal 2008（国際鳥類内分泌学会）
 Bargmann-Scharrer Award 2013（国際比較内分泌学会連合）
 文部科学大臣表彰・科学技術賞 2015（文部科学省）
 国際小脳学会功労賞 2015（国際小脳学会）
 大隈記念学術褒賞 2015（早稲田大学）
 小林賞 2016（日本比較内分泌学会）

◆ 主な学術活動 ◆

会 長： 国際比較内分泌学会連合
 会 長： 国際鳥類内分泌学会
 前会長： アジア・オセアニア比較内分泌学会
 元会長： 日本比較内分泌学会
 科学顧問： 国際小脳学会
 副会長： 日本動物学会
 理 事： 日本生殖内分泌学会
 評議員： 国際鳥学会連合，国際両生類・爬虫類内分泌学神経科学会議，国際神経ペプチド学会
 Editor-in-chief: Current Metabolomics and Systems Biology
 Editor: Frontiers in Neuroendocrine Science; Front in Experimental Endocrinology; General and Comparative Endocrinology; Brain, Behavior and Immunity; PeerJ; Hormonal Studies; Physiology Journal; BioMed Research International
 Editorial Board: Endocrinology; Journal of Neuroendocrinology; Scientific Reports, Frontiers in Integrative Pharmacology; Journal of Experimental Neuroscience; Neuroendocrinology Letters; Open Journal of Neuroscience; Animal Cells Systems; European Journal of Zoology
 編集主幹： 日本生殖内分泌学会雑誌

◆ 最近の科学研究費取得状況 ◆

科学研究費（基盤研究 S）（代表）平成 22-26 年度
 「生殖制御における新規脳内分子機構の解明」
 科学研究費（基盤研究 S）（代表）平成 18-21 年度

「新規脳分子による新しい生殖制御機構の解明」

科学研究費（特定領域研究）（代表）平成 16-20 年度

「ニューロステロイドによる脳の性分化メカニズム」

科学研究費（基盤研究 A1）（代表）平成 15-17 年度

「新規視床下部ホルモンによる脳下垂体ホルモン合成・放出の新しい制御機構」

◆ 英文原著・総説論文抜粋（最近 10 年間の抜粋）◆

- S. Haraguchi, K. Tsutsui, et. (2019) Light-at-night exposure affects brain development through pineal allopregnanolone-dependent mechanisms. *eLife* 8: e45306 (*IF*=8.5)
- M. Nozaki, K. Tsutsui, et. Expression of steroidogenic enzymes and metabolism of steroids in COS-7 cells known as non-steroidogenic cells. *Scientific Reports* 8: 2167 (*IF*=5.1)
- K. Tsutsui, et al. (2017) Review: Discovery of GnIH and its role in hypothyroidism-induced delayed puberty. *Endocrinology* doi: 10.1210/en.2017-00300. (*IF*=5.0)
- J. Leprince, K. Tsutsui, et. (2017) IUPHAR Review: The Arg-Phe-amide peptide 26RFa/QRFP and its receptor. *British J. Pharmacol.* 174: 3573-3607. (*IF*=5.3)
- M. Kiyohara, Y. L. Son and K. Tsutsui (2017) Involvement of gonadotropin-inhibitory hormone in pubertal disorders induced by thyroid status. *Scientific Reports* 217: 1042. (*IF*=5.1)
- Y. L. Son, T. Ubuka, T. Soga, K. Yamamoto, G. E. Bentley and K. Tsutsui (2016) Inhibitory action of gonadotropin-inhibitory hormone on the signaling pathways induced by kisspeptin and vasoactive intestinal polypeptide in GnRH neuronal cell line, GT1-7. *FASEB J.* 30: 2198-210. (*IF*=5.1)
- S. Haraguchi, Y. Yamamoto, Y. Suzuki, J. H. Chang, T. Koyama, M. Sato, M. Mita, H. Ueda and K. Tsutsui (2015) 7 α -Hydroxypregnenolone, a key neuronal modulator of locomotion, stimulates upstream migration by means of the dopaminergic system in salmon. *Scientific Reports* 5: 12546. (*IF*=5.1)
- L. J. Kriegsfeld, T. Ubuka and K. Tsutsui (2015) Review: Seasonal control of gonadotropin-inhibitory hormone (GnIH) in birds and mammals. *Front. Neuroendocrinol.* 37: 65-75. (*IF*=12.8)
- T. Sasanami, T. Yoshimura, K. Ukena and K. Tsutsui (2015) A unique mechanism of successful fertilization in a domestic bird. *Scientific Reports* 5: 7700. doi: 10.1038/srep07700. (*IF*=5.1)
- Y. Tobari, Y. L. Son, T. Ubuka, Y. Hasegawa and K. Tsutsui (2014) A new pathway mediating social effects on the endocrine system: female presence acting via norepinephrine release stimulates gonadotropin-inhibitory hormone in the paraventricular nucleus and suppresses luteinizing hormone in quail. *J. Neurosci.* 34: 9803-9811. (*IF*=8.2)
- Y. L. Son, T. Ubuka, M. Narihiro, Y. Fukuda, I. Hasunuma, K. Yamamoto, D. D. Belsham and

- K. Tsutsui** (2014) Molecular basis for the activation of gonadotropin-inhibitory hormone gene transcription by corticosterone. *Endocrinology* 155: 1817–26. (IF=5.0)
- T. Ubuka, S. Haraguchi, Y. Tobari, M. Narihiro, K. Ishikawa, T. Hayashi, N. Harada and **K. Tsutsui** (2014) Hypothalamic inhibition of socio-sexual behaviour by increasing neuroestrogen synthesis. *Nature Communications* 5: Article number 3061 doi: 10.1038/ncomms4061 (IF=10.0)
- T. Osugi, N. Ohtaki, Y. Sunakawa, Y. L. Son, M. Ohkubo, M. Amano and **K. Tsutsui** (2013) Molecular evolution of Kiss2 genes and peptides in vertebrates. *Endocrinology* 154: 4270–4280. (IF=5.0)
- K. Tsutsui**, S. Haraguchi, Y. Fukada and H. Vaudry (2013) Review: Brain and pineal 7 α -hydroxypregnenolone stimulating locomotor activity: identification, mode of action and regulation of biosynthesis. *Front. Neuroendocrinol.* 34: 179–189. (IF=12.8)
- F. Maekawa, **K. Tsutsui**, et. (2013) A genetically female brain is required for a regular reproductive cycle in chicken brain chimeras. *Nature Communications* 4: Article number 1372 doi: 10.1038/ncomms2372. (IF=10.0)
- S. Haraguchi, S. Hara, T. Ubuka, M. Mita and **K. Tsutsui** (2012) Possible role of pineal allopregnanolone in Purkinje cell survival. *Proc. Natl. Acad. Sci. USA* 109: 21110–21115. (IF=9.8) *MDLinx* 4345182 January 9, 2013
- T. Osugi, T. Kosugi, T. Ubuka, K. Gazda, D. Daukss, M. Nozaki, S. A. Sower and **K. Tsutsui** (2012) Evolutionary origin of the structure and function of gonadotropin-inhibitory hormone: Insights from lampreys. *Endocrinology* 153: 2362–2374. (IF=5.0)
- Y. L. Son, T. Ubuka, R. P. Millar and **K. Tsutsui** (2012) Gonadotropin-inhibitory hormone inhibits gonadotropin-releasing hormone-induced gonadotropin synthesis mediated by adenylate cyclase/cAMP/PKA-dependent ERK pathway in L β T2 gonadotrope cells. *Endocrinology* 153: 2332–2343. (IF=5.0) *Global Medical Discovery: Key Scientific Article* June 18, 2012
- S. Haraguchi, T. Koyama, I. Hasunuma, T. Ubuka, S. Kikuyama, J. L. Do Rego, H. Vaudry and **K. Tsutsui** (2012) Acute stress increases the synthesis of 7 α -hydroxypregnenolone, a new key neurosteroid stimulating locomotor activity, through corticosterone action. *Endocrinology* 153: 794–805. (IF=5.0)
- T. Ubuka, K. Inoue, K. Ukena, L. J. Kriegsfeld and **K. Tsutsui** (2012) Identification, expression, and physiological functions of Siberian hamster gonadotropin-inhibitory hormone. *Endocrinology* 153: 373–385. (IF=5.0)
- T. Osugi, K. Uchida, M. Nozaki and **K. Tsutsui** (2011) Characterization of novel RFamide peptides in the central nervous system of the brown hagfish: isolation, localization, and functional analysis. *Endocrinology* 152: 4252–4264. (IF=5.0) *News and Views* (2011) Hagfish, genome duplications,

- and RFamide neuropeptide evolution. *Endocrinology* 152: 4010–4013.
- M. Hatori, **K. Tsutsui**, et. (2011) Light-dependent and circadian clock-regulated activation of SREBP, XBP1 and HSF pathways in the pineal gland. *Proc. Natl. Acad. Sci. USA* 108: 4864–4869. (IF=9.8)
- K. Tsutsui**, G. E. Bentley, L. J. Kriegsfeld, T. Osugi, J. Y. Seong, and H. Vaudry (2010) Review: Discovery and evolutionary history of GnIH and kisspeptin: New key neuropeptides controlling reproduction. *J. Neuroendocrinol* 22: 716–727. (IF=4.7)
- K. Tsutsui**, G. E. Bentley, G. Bedecarrats, T. Osugi, T. Ubuka, L. J. Kriegsfeld (2010) Review: Gonadotropin-inhibitory hormone (GnIH) and its control of central and peripheral reproductive function. *Front. Neuroendocrinol.* 31: 284–295. (IF=12.8)
- K. Ukena, T. Tachibana, E. Iwakoshi-Ukena, Y. Saito, H. Minakata, R. Kawaguchi, T. Osugi, Y. Tobari, J. Leprince, H. Vaudry and **K. Tsutsui** (2010) Identification, localization and function of a novel avian hypothalamic neuropeptide, 26RFa, and its cognate receptor, GPR103. *Endocrinology* 151: 2255–2264. (IF=5.0)
- S. Haraguchi, T. Koyama, I. Hasunuma, H. Vaudry and **K. Tsutsui** (2010) Prolactin increases the synthesis of 7α -hydroxypregnenolone, a key factor for induction of locomotor activity, in breeding male newts. *Endocrinology* 151: 2211–2222. (IF=5.0)
- M. Doi, **K. Tsutsui** et. (2010) Salt-sensitive hypertension in circadian clock-deficient *Cry*-null mice involves dysregulated adrenal Hsd3b6. *Nature Medicine* 16: 67–74. (IF=27.6) *Faculty of 1000 Must Read*
- V. S. Chowdhury, K. Yamamoto, T. Ubuka, G. E. Bentley, A. Hattori and **K. Tsutsui** (2010) Melatonin stimulates the release of gonadotropin-inhibitory hormone by the avian hypothalamus. *Endocrinology* 151: 271–280. (IF=5.0) *Endocrine news* Vol. 34 No. 12, p. 7 (Dec. 2009)
- K. Tsutsui** (2009) Review: A new key neurohormone controlling reproduction, gonadotropin-inhibitory hormone (GnIH): Biosynthesis, mode of action and functional significance. *Prog. Neurobiol.* 88: 76–88. (IF=11.3) *Selected for Issue Cover*
- Y. R. Lee, K. Tsunekawa, M. J. Moon, H. N. Um, J.-I. Hwang, T. Osugi, N. Otaki, Y. Sunakawa, K. Kim, H. Vaudry, H. B. Kwon, J. Y. Seong and **K. Tsutsui** (2009) Molecular evolution of multiple forms of kisspeptins and GPR54 receptors in vertebrates. *Endocrinology* 150: 2837–2846. (IF=5.0)
- J. L. Do Rego, J. Y. Seong, D. Burel, J. Leprince, V. Luu-The, **K. Tsutsui**, M.-C. Tonon, G. Pelletier and Hubert Vaudry (2009) Review: Neurosteroid biosynthesis: enzymatic pathways and neuroendocrine regulation by neurotransmitters and neuropeptides. *Front. Neuroendocrinol.* 30: 259–301. (IF=12.8)
- K. Tsutsui** (2008) Review: Neurosteroids in the Purkinje cell: Biosynthesis, mode of action and

functional significance. *Mol. Neurobiol.* 37: 116–125. (IF=6.1)

- K. Tsutsui, K. Inoue, H. Miyabara, Y. Ogura and S. Haraguchi (2008) 7α -Hydroxypregnenolone mediates melatonin action underlying diurnal locomotor rhythms. *J Neuroscience* 28: 2158–2167. (IF=8.2)
- K. Tsutsui (2008) Review: Progesterone biosynthesis and action in the developing neuron. *Endocrinology* 149: 2757–2761. (IF=5.0)
- T. Ubuka, S. Kim, Y. Huang, J. Reid, J. Jiang, T. Osugi, V. S. Chowdhury and K. Tsutsui (2008) Gonadotropin-inhibitory hormone neurons interact directly with gonadotropin-releasing hormone-I and -II neurons in European starling brain. *Endocrinology* 149: 268–278. (IF=5.0)
Endocrine news p. 11
- K. Sasahara, H. Shikimi, S. Haraguchi, H. Sakamoto, S. Honda, N. Harada and K. Tsutsui (2007) Mode of action and functional significance of estrogen inducing dendritic growth, spinogenesis and synaptogenesis in the developing Purkinje cell. *J Neuroscience* 27: 7408–7417. (IF=8.2)
- T. Ubuka, K. Ukena, P. J. Sharp, G. E. Bentley and K. Tsutsui (2006) Gonadotropin-inhibitory hormone inhibits gonadal development and maintenance by decreasing gonadotropin synthesis and release. *Endocrinology* 147: 1187–1194. (IF=5.0)
- L. J. Kriegsfeld, K. Tsutsui, et. (2006) Identification and characterization of a gonadotropin-inhibitory system in the brains of mammals. *Proc. Natl. Acad. Sci. USA* 103: 2410–2415. (IF=9.8)
Faculty of 1000 Recommended
- K. Tsutsui and S. H. Mellon (2006) Neurosteroids in the brain neuron: Biosynthesis, action and medicinal impact on neurodegenerative disease. *Central Nerv. Syst. Agents Med. Chem.* 6: 73–82. (IF=5.0)
- T. Ubuka, G. E. Bentley, K. Ukena, J. C. Wingfield and K. Tsutsui (2005) Melatonin induces the expression of gonadotropin-inhibitory hormone in the avian brain. *Proc. Natl. Acad. Sci. USA* 102: 3052–3057. (IF=9.4) *Nature Reviews Highlight [Nat. Rev. Neurosci.* 6: 264–265 (2005)]
- K. Ukena and K. Tsutsui (2005) Review: A new member of the hypothalamic RF-amide peptide family, LPXRF-amide peptides: Structure, localization and function. *Mass Spectrom. Rev.* 24: 469–486. (IF=11.5)
- M. Matsunaga, K. Ukena and K. Tsutsui (2004) 7α -Hydroxypregnenolone acts as a neuronal activator to stimulate locomotor activity of breeding newts by means of the dopaminergic system. *Proc. Natl. Acad. Sci. USA* 101: 17282–17287. (IF=9.8)
- H. Sakamoto, K. Ukena and K. Tsutsui (2001) Effects of progesterone synthesized *de novo* in the developing Purkinje cell on its dendritic growth and synaptogenesis. *J. Neuroscience* 21: 6221–6232. (IF=8.2)

- K. **Tsutsui**, E. Saigoh, K. Ukena, H. Teranishi, Y. Fujisawa, M. Kikuchi, S. Ishii and P. J. Sharp (2000)
A novel avian hypothalamic peptide inhibiting gonadotropin release. *Biochem. Biophys. Res. Commun.* 275: 661–667. (*IF*=3.6)
- K. Ukena, M. Usui, C. Kohchi and K. **Tsutsui** (1998) Cytochrome P450 side-chain cleavage enzyme in the cerebellar Purkinje neuron and its neonatal change in rats. *Endocrinology* 139: 137–147. (*IF*=5.0)